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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/788,051	02/16/2001	Shubhada D. Godbole	HYS-39	6652

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EXAMINER	
HADDAD, MAHER M	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 12/30/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/788,051	GODBOLE ET AL.	
	Examiner	Art Unit	
	Maher M. Haddad	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 October 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-29* is/are pending in the application.

4a) Of the above claim(s) *1-8,13-23 and 25-29* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *9-12 and 24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. The Art Unit location and the examiner of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Maher Haddad, Art Unit 1644, Technology Center 1600.

2. Claims 1-29 are pending.

3. Applicant's election without traverse of Group II, claims 9-12 and 24 drawn to an isolated polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 4 and 6-15 filed on 10/21/04, is acknowledged.

4. Claims 1-8, 13-23, 25-29 are withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to nonelected inventions.

5. Claims 9-12 and 24 are under examination as they read on an isolated polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 4 and 6-15.

6. The specification on page 1 should be amended to reflect the status of 09/560,875 and 09/496,914 the relationship between these applications and the instant application.

7. The specification on page 10, lines 22-23 and 29-30, is objected to because it disclsoes that "the two sequences share 81% similarity over **nucleotides** 283-1539 of SEQ ID NO:4 and 64% identity over the **nucleotides** 283-1539 of SEQ ID NO:4". First, SEQ ID NO:4 is an amino acid sequence comprising 636 amino acids and is limited to its amino acids componants. Second, is is unclear how a 636 amino acid sequence of SEQ ID NO: 4 would have 1539 amino acids.

8. Claim 11 is objected to because of the following informalties: Claim 11 recites "from the group consisting of SEQ ID NO: SEQ ID NO:". One of the two "SEQ ID NO:" should be deleted. Correction is required.

9. The following is a quotation of the second paragraph of 35 U.S.C. 112.

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claim 9-12 and 24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. The "translated protein coding portion thereof", and "mature protein" recited in claim 9 has no antecedent. It is unclear which protein is being claimed.

B. The "cadherin-like activity" recited in claim 11 is indefinite. It is unclear which "activity" is contemplated.

C. Claims 11 and 12 are indefinite in the recitation "at least twenty" and " at least twenty five amino acids", respectively because SEQ ID NO: 6, 11, 12, 14 consist of only 16, 18, 18 and 16 amino acids, respectively. It is unclear how a 16 or 18 amino acid sequence would comprise at least 20 or 25 amino acids.

11. 35 U.S.C. §101 states:

> *Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.*

12. Claims 11-12 are rejected under 35 USC 101 because the claimed invention is directed to non-statutory subject matter.

Claims 11-12, as written, do not sufficiently distinguish over nucleic acids, proteins, cells and antibodies as they exist naturally because the claims do not particularly point out any non-naturally occurring differences between the claimed products and the naturally occurring products. In the absence of the hand of man, the naturally occurring products are considered non-statutory subject matter. *See Diamond v. Chakrabarty*, 447 U.S. 303, 206 USPQ 193 (1980). The claims should be amended to indicate the hand of the inventor, e.g., by insertion of "Isolated" as recited in claim 9. See MPEP 2105.

13. Claims 9-12 and 24 are rejected to under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and/or substantial asserted utility or a well established utility.

Applicants are directed to the Final Utility Guidelines, Federal Register, and Published Friday January 5, 2001.

The instant application has provided a description of an isolated polypeptide. The instant application does not disclose the biological role of the polypeptide or its significance. The specification on page 4, lines 12-13 discloses that the encoded polynucleotides of the present invention are based on a cadherin-like polynucleotide isolated from human umbilical cord mRNA. The instant specification asserts specific utilities for the claimed invention, for diagnostics, forensics, gene mapping; identification of mutations responsible for genetic disorders or other traits, to asses biodiversity, and to produce many other types of data and products dependent on DNA and amino acid sequences (on page 1, lines 21-24 in particular).

The specification also asserts that the claimed cadherin-like protein is acknowledged by the Applicants to be useful in the treatment of cancers like osteosarcoma, breast cancer, endocrine tumors, and also to treat bone and cartilage-related metabolic diseases like osteoporosis, Paget's disease, osteomalacia, hyperostosis, and osteopetrosis (see page 4, lines 1-3 in particular) and cadherin proteins present on the cell membranes are disclosed to be act as receptors for hormones and cytokines, they provide adhesive interactions for a cell to attach to extracellular matrix; highly glycosylated proteins form a glycocalyx around the cell that maintains the repulsive charge barrier; and many proteins serve as counter-receptors for receptors on other cells to communicate with the other cell (page 2, lines 1-5 in particular), among others. Further, the specification asserts that cadherins share a common cadherin domain in their extracellular region, which mediates homotypic cell-cell adhesion that is calcium-dependent (see page 2, lines 13-15 in particular).

These utilities are not considered to be specific and substantial because the specification fails to disclose any particular function or biological significance for the cadherin-like polypeptide. The disclosed polypeptide is said to have a potential function based upon its amino acid sequence similarity to other known proteins. After further research, specific and substantial utility might be found for the claimed isolated compositions. This further characterization, however, is part of the act of invention and until it has been undertaken, Applicant's claimed invention is incomplete.

Assignment to a prior art family of proteins is insufficient to meet the utility requirement unless such assignment would allow the artisan to assign a specific and substantial use to the new member of the protein family. Okazaki et al teach that several rat cadherin genes obtained by the PCR cloning, one of which clone 11, shows strong similarity to OB-cadherin (97% identity over 510 residues compared). It is still questionable whether clone 11 is a rat counterpart of OB-cadherin because of the different RNA expression pattern in tissues (see page 12097, 2nd col., 2nd paragraph under Discussion in particular). Since the specification fails to teach a specific function of the recited sequence, sequence homology alone is insufficient to provide a use for claimed SEQ ID NO: 4.

The instant situation is directly analogous to that which was addressed in *Brenner V. Manson*, 148 U.S. P. Q. 689 (1966), in which a novel compound which was structurally analogous to other compounds which were known to possess anti-tumor activity was alleged to be potentially useful as an anti-tumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation. However, the court held that this broad interpretation was not the intended definition of "useful" as it appears in 35 U.S. C. § 101, which requires that an invention must have either an immediatedly apparent or fully disclosed "real world" utility. The instant claims are drawn to a polypeptide of as yet undetermined function or biological significance. There is no evidence of record or any line of reasoning that would support a conclusion that the claimed cadherin-like of SEQ ID NO: 4 of the instant application was, as of the filling date, useful for treating cancers, osteoporosis, Paget's disease, osteomalacia, hyperostosis and osteopetrosis as stated at pages 4 of the specification. Until some actual and

specific significance can be attributed to the protein identified in the specification as cadherin-like polypeptide, one of ordinary skill in the art would be required to perform additional experimentation in order to determine how to use the claimed invention. Thus, there was no immediately apparent or "real world" utility as of the filing date.

The instant application has failed to provide guidance as to how one of skill in the art could use the claimed invention in a way that constitutes a specific and substantial utility. The proposed uses of the claimed invention are simply starting points for further research and investigation into potential practical uses of the cadherin-like polypeptide. "Congress intended that no patent be granted on a chemical compound whose sole 'utility' consists of its potential role as an object of use-testing." Brenner v. Manson, 148 USPQ at 696.

The nucleic acid of the instant invention and the protein encoded thereby are compounds which share 81% structural similarity of its amino acids 45-463 over amino acids 283-1539 of human OB-cadherin-1/OSF-4-1 proteins based on sequence similarity. It is not clear if the protein of the instant application would have the same function as OB-cadherin/OSF-4-1. The instant specification fails to disclose, beyond the predicted polypeptide sequence, other structural characteristics that are shared by the cadherin family, the expression patterns, the tissue distribution and whether it possesses the functional similarity of OB-cadherin. Attwood (Science 2000; 290:471-473) teaches that "[i]t is presumptuous to make functional assignments merely on the basis of some degree of similarity between sequences. Similarly, Skolnick et al. (Trends in Biotech. 2000; 18(1):34-39) teach that the skilled artisan is well aware that assigning functional activities for any particular protein or protein family based upon sequence homology is inaccurate, in part because of the multifunctional nature of proteins (e.g., "Abstract" and "Sequence-based approaches to function prediction", page 34). Even in situations where there is some confidence of a similar overall structure between two proteins, only experimental research can confirm the artisan's best guess as to the function of the structurally related protein (see in particular "Abstract" and Box 2). To employ a protein of the instant invention in any of the disclosed methods would clearly be using it as the object of further research. Such a use has been determined by the courts to be a utility which, alone, does not support patentablility. Since the instant specification does not disclose a "real world" use for the claimed cadherin-like polypeptide of SEQ ID NO: 4, then the claimed invention as disclosed does not meet the requirement of 35 U.S.C. § 101 as being useful.

14. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

15. Claims 9-12 and 24 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and/or substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would

not know how to use the claimed invention so that it would operate as intended without undue experimentation.

Further, besides the isolated polypeptide or a kit comprising of SEQ ID NO: 4 or a polypeptide consisting of SEQ ID NOs:6-15 the specification fails to provide any guidance as to how to make any isolated polypeptide "comprising" an amino acid sequence which is "at least 95% identical" to the amino acid sequence selected from the group consisting of SEQ ID NO: 4 and 6 or "the translated protein coding portion thereof", "the mature protein coding portion thereof", the "extracellular portion thereof" or the "active domain thereof" in claim 9, or a composition comprising the polypeptide in claim 10, or a polypeptide, having cadherin activity, "comprising" at "at least twenty consecutive amino acids" from the polypeptide sequences selected from the group consisting of SEQ ID NO: 4 and 6-15 in claim 11, the polypeptide "comprising" "at least twenty five consecutive amino acids" from the polypeptide sequences selected from the group consisting of SEQ ID NO:4 and 6-15 in claim 12, or a kit comprising the polypeptide of claim 11 in claim 24. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with this claim.

The specification does not provide a sufficient enabling description of the claimed invention. The specification discloses only a single nucleic acid sequence (SEQ ID NO:4) encoding a single polypeptide (SEQ ID NO:4) and fragments thereof consisting of SEQ ID NO: 6-15. The instant claims encompass in their breadth *any* polypeptide with at least 95% identity to SEQ ID NO:4 or 6"; or *any* polypeptide that comprises at least "twenty/twenty five consecutive amino acids" of SEQ ID NO: 4 or 5-15.

The terms "comprises" and "comprising" in claims 9 and 11-12 are open ended and extend the claimed polypeptide to include additional non-recited amino acids on either or both C-terminal or N-terminal of SEQ ID NOS: 6-15. It has been well known to those skilled in the art at the time the invention was made that minor structural differences among structurally related compounds or compositions can result in substantially different biological activities. Without detailed direction as to which amino acid sequences are essential to the function of the polypeptide, a person of skill in the art would not be able to determine without undue experimentation which of the plethora of amino acid sequences encompassed by the instant claims would share the same function as OB-cadherin.

The instant claims language encompasses fragments. For example, claim 9 recites a "translated protein coding portion", the "mature protein coding portion", the extracellular portion" or the "active domain", claim 11 recites "at least twenty consecutive amino acids" and claim 12 recites "at least twenty five consecutive amino acids". Such a recitation does not require that the full length of amino acid sequence set forth in SEQ ID NO:4; but rather encompasses any amino acid sequence comprising either the full length of SEQ ID NO:4 or *any fragment*. However, the specification does not appear to have provided sufficient guidance as to which subsequences of SEQ ID NO:4 would share the function of OB-cadherin. Neither

does the specification appear to have provided any working examples of any functional fragments/homologue of the fragments. Thus it would require undue experimentation of the skilled artisan to determine which subsequences of SEQ ID NO:4 would have the function of the full length molecule.

Claim 9 recites "at least 95% identical". The claims as written encompass a broad genus of polypeptides with an unlimited number of possibilities with regard to the length of the polypeptide sequence. Further, the enablement issues of making the protein remains because the specification does not teach and provide sufficient guidance as to which amino acid of SEQ ID NOs: 4 and 6 would have been altered such that the resultant polypeptide would have retained the claimed function. In addition, variation up to 5% of SEQ ID NO: 4 (32^{20}) provide a range of activities, not all which are necessarily predictive of the claimed function. Therefore, absent the ability to predict which of these polypeptides would function as claimed, and given the lack of data on regions critical for activity, for one of skill in the art to practice the invention as claimed would require a level of experimentation that is excessive and undue.

It is recognized in the prior art that the function of a protein depends on the sequence of its amino acids in a certain pattern, conformation of the protein due to the amino acid sequence and the functional properties of the different parts of the protein. The specification does not teach which changes in the amino acid of SEQ ID NOs:4 and 6 would not alter all the activities of the polypeptides. Therefore, the specification fails to provide sufficient guidance as to which core structure of SEQ ID NO: 4 is essential for maintain its biological activity and which changes can be made in the structure of SEQ ID NO: 4 and still maintained the same function.

Attwood (Science 2000; 290:471-473) teaches that "[i]t is presumptuous to make functional assignments merely on the basis of some degree of similarity between sequences. Similarly, Skolnick et al. (Trends in Biotech. 2000; 18(1):34-39) teach that the skilled artisan is well aware that assigning functional activities for any particular protein or protein family based upon sequence homology is inaccurate, in part because of the multifunctional nature of proteins (e.g., "Abstract" and "Sequence-based approaches to function prediction", page 34). Even in situations where there is some confidence of a similar overall structure between two proteins, only experimental research can confirm the artisan's best guess as to the function of the structurally related protein (see in particular "Abstract" and Box 2). Finally, even single amino acid differences can result in drastically altered functions between two proteins. Thus it is unpredictable if any functional activity will be shared by two polypeptides having less than 100% identity over the full length of their sequences.

Reasonable correlation must exist between the scope of the claims and scope of enablement set forth. In view of the quantity of experimentation necessary, the limited working examples, the unpredictability of the art, the lack of sufficient guidance in the specification, and the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

16. Claims 9-12 and 24 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant is in possession of an isolated polypeptide comprising SEQ ID NO:4, a composition and a kit thereof and a polypeptide consisting of SEQ ID NO:6-15.

Applicant is not in possession of any isolated polypeptide "comprising" an amino acid sequence which is "at least 95% identical" to the amino acid sequence selected from the group consisting of SEQ ID NO: 4 and 6 or "the translated protein coding portion thereof", "the mature protein coding portion thereof", the "extracellular portion thereof" or the "active domain thereof" in claim 9, or a composition comprising the polypeptide in claim 10, or a polypeptide, having cadherin activity, "comprising" at "at least twenty consecutive amino acids" from the polypeptide sequences selected from the group consisting of SEQ ID NO: 4 and 6-15 in claim 11, the polypeptide "comprising" "at least twenty five consecutive amino acids" from the polypeptide sequences selected from the group consisting of SEQ ID NO:4 and 6-15 in claim 12, or a kit comprising the polypeptide of claim 11 in claim 24.

Applicant has disclosed only amino acid of SEQ ID NO: 4 and the fragments of SEQ ID NO: 6-15; therefore, the skilled artisan cannot envision all the contemplated amino acid sequence possibilities recited in the instant claims. Consequently, conception cannot be achieved until a representative description of the structural and functional properties of the claimed invention has occurred, regardless of the complexity or simplicity of the method. Adequate written description requires more than a mere statement that it is part of the invention. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC1993). The Guidelines for the Examination of Patent Application Under the 35 U.S.C.112, ¶ 1"Written Description" Requirement make clear that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 20001, see especially page 1106 3rd column).

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.). Consequently, Applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.

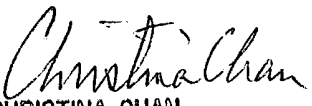
Applicant is directed to the final Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

17. No claim is allowed.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maher Haddad whose telephone number is (571) 272-0845. The examiner can normally be reached Monday through Friday from 7:30 am to 4:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Maher Haddad, Ph.D.
Patent Examiner
Technology Center 1600
December 22, 2004



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